

REMARKS

The amendment to the claims is voluntary and made at the option of the assignee as being of commercial interest for immediate patent protection. Applicants intend to pursue coverage for the subject matter previously claimed in one or more separate applications.

Entry of the claim amendments does not introduce new matter into the disclosure. Support for the new claims may be found at various places in the specification, such as the following:

Claim 21:	Previous claims 1 & 2; page 3 lines 32-35; page 12 lines 29-31; page 13 lines 24-28; page 19 line 32 to page 20 line 25; Table 3 (page 22); Table 4 (page 23); Example 3 (page 24); Example 8 (page 27 ff.); and throughout the disclosure.
Claims 22-25:	Page 11 lines 22-29; Example 1 (page 22 ff.); Table 3 (page 22); Example 8 (page 31 ff.)
Claim 26:	Page 11 lines 14-19
Claim 27	Page 11 line 41 to page 12 line 1
Claims 28-29:	Page 11 line 40 to page 12 line 5; page 23 lines 11-13; page 27 lines 32-35.
Claim 30:	Page 12 lines 11-31; Example 1 (page 22 ff.)
Claims 31-32:	Page 12 lines 29-31
Claims 33:	Table 5 (page 25)
Claims 34:	Example 8 (pages 27-29)
Claim 35:	Page 13 lines 5-13
Claim 36:	Page 13 lines 19-23
Claim 37:	Page 14 lines 15-18
Claim 38:	Page 14 lines 19-22
Claim 49:	Table 7 (page 29)
Claim 40:	Page 13 line 15 to page 14 line 28; Example 6 (page 25 lines 15-35); Table 7 (page 29)

Claim 41:	Previous claim 8
Claim 42:	Previous claim 9
Claim 43:	Previous claim 1
Claim 44:	Previous claims 3 & 4
Claim 45:	Previous claim 5
Claim 46:	Page 19 lines 18-23; Example 4 (page 25 ff)

Applicants respectfully request examination of the application on the merits in view of these amendments.

#### Interview Summary

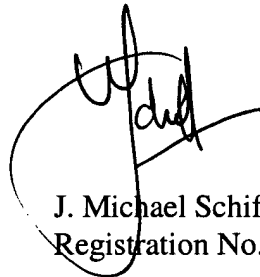
The undersigned acknowledges with gratitude the telephone conversation with the Examiner on January 17, 2002, with regards to the filing of this Preliminary Amendment. The particulars in the Interview Summary mailed January 23, 2002 (Paper 3) are correct. This paragraph is included in this Amendment in compliance with Box (i) on Paper 3.

Conclusion

Applicants have previously paid for examination of 20 claims in this application. The new claim set contains 26 claims, of which 1 is independent. Authorization to charge Deposit Account No. 07-1139 for fee for examination of an additional 6 claims is provided on the accompanying transmittal.

Nevertheless, should the Patent Office determine that an additional fee is required for further consideration of the application, the Assistant Commissioner is hereby authorized to charge such fee (or credit any overpayment) to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "J. Michael Schiff", is written over a circular stamp or seal.

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Version with Markings to show  
**CHANGES MADE**

*USSN 09/872,183*  
*Docket 094/004*

***Amendment to the TITLE***

**~~NEURAL PROGENITOR CELL POPULATIONS~~**

**MAKING NEURAL CELLS FOR HUMAN THERAPY OR DRUG SCREENING  
FROM HUMAN EMBRYONIC STEM CELLS**

***Claim amendments***

*Cancel Claims 1-20 and substitute therefor the following:*

21. *(New)* A method for producing a neural cell population from human embryonic stem (hES) cells, comprising culturing progeny of the ES cells in a medium containing one or more added neurotrophins and one or more added mitogens, thereby producing a population in which at least 60% of the cells express A2B5, polysialylated NCAM, MAP-2, or Nestin.
22. *(New)* The method of claim 21, wherein the added neurotrophins include neurotrophin 3 (NT-3) or brain-derived neurotrophic factor (BDNF).
23. *(New)* The method of claim 22, wherein the added neurotrophins include both NT-3 and BDNF.
24. *(New)* The method of claim 21, wherein the added mitogens include a mitogen selected from epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF), and insulin-like growth factor 1 (IGF-1).
25. *(New)* The method of claim 24, wherein the added mitogens include both PDGF and IGF-1.
26. *(New)* The method of claim 21, wherein the progeny are cultured on fibronectin.
27. *(New)* The method of claim 21, comprising pre-differentiating the hES cells in a medium containing retinoic acid [or equivalents] before culturing with the neurotrophins and mitogens.
28. *(New)* The method of claim 21, comprising pre-differentiating the hES cells by forming embryoid bodies before culturing with the neurotrophins and mitogens.
29. *(New)* The method of claim 21, comprising propagating progeny of the hES cell line as cell aggregates.
30. *(New)* The method of claim 21, comprising selecting and propagating cells that are positive for polysialylated NCAM.

31. (New) The method of claim 21, wherein the produced cell population is at least 60% positive for polysialylated NCAM.
32. (New) The method of claim 21, wherein the produced cell population is at least 90% positive for polysialylated NCAM.
33. (New) The method of claim 21, wherein the produced cell population is at least 38%  $\beta$ -tubulin III positive.
34. (New) The method of claim 21, wherein the produced cell population has the characteristic that culturing it in the presence of neurotrophins maintains capacity of the cells to proliferate and to form tyrosine hydroxylase positive neurons upon differentiation.
35. (New) The method of claim 21, wherein the produced cell population is essentially free of undifferentiated hES cells.
36. (New) The method of claim 21, further comprising differentiating the cells into a population that contains at least 30% neurons.
37. (New) The method of claim 21, further comprising differentiating the cells into a population that contains at least 30% MAP-2 positive cells.
38. (New) The method of claim 37, wherein at least 3% of the differentiated cells positive for MAP-2 are also positive for tyrosine hydroxylase.
39. (New) The method of claim 37, wherein at least 8% of the differentiated cells positive for MAP-2 are also positive for tyrosine hydroxylase.
40. (New) The method of claim 37, wherein the differentiating comprises culturing the cells in a medium containing one or more factors selected from neurotrophins, cAMP, and ascorbic acid for at least 3 days, in the absence of added mitogens.
41. (New) The method of claim 21, wherein the differentiated cell population comprises sensory or motor neurons.
42. (New) The method of claim 21, wherein the differentiated cell population comprises oligodendrocytes or astrocytes.
43. (New) The method of claim 21, further comprising combining the cell population with a compound, determining any phenotypic or metabolic changes in the cell that result from contact with the compound, and correlating the change with cellular toxicity or modulation caused by the compound.
44. (New) The method of claim 43, comprising determining whether the compound is toxic to cells in the population, or affects ability of cells in the population to be maintained in culture.
45. (New) The method of claim 43, comprising determining whether the compound changes neurotransmitter synthesis, release, neurotransmitter uptake, or electrophysiology by cells in the population.
46. (New) The method of claim 21, further comprising combining the cells with a pharmaceutically compatible excipient.